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FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,769	HOEFFLER ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2003 and 22 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-22 and 24-54* is/are pending in the application.

4a) Of the above claim(s) *9-18 and 30-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,19-22,24-29 and 46-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20010828;20020110*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS-20020625; Notice to Comply*.

DETAILED ACTION

1. The election filed July 22, 2003 is acknowledged and has been entered. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In reply to the Office action mailed January 28, 2003, which set forth a first restriction and election requirement, Applicant has elected the invention of Group I, claims 1-7, 19-22, 24-29, and 46-53, drawn to methods of screening a DNA construct library, kits, expression vectors, DNA constructs, classified in class 435,

In reply to the Office action mailed June 5, 2003, which set forth a second restriction and election requirement, Applicant has elected the species of the invention of claims 1-7, 20-22, 24-29, and 46-53, wherein said transcription associated biomolecule of claims 1, 20, 24, and 25 is a nuclear hormone receptor or the DNA binding domain thereof.

2. The amendment filed July 22, 2003 is acknowledged and has been entered. Claims 4, 6, and 22 have been amended.

3. The amendment filed August 15, 2003 is acknowledged and has been entered. Claim 19 has been amended. Claim 54 has been added.

4. Claims 1-7, 9-22, and 24-54 are pending in the application. Claims 9-18 and 30-45 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species of invention, there being no allowable generic or linking claim.

5. Claims 1-7, 19-22, 24-29, and 46-54 are currently under prosecution.

Election/Restrictions

6. Upon reconsideration, the requirement to elect a species of invention by identifying one of the transcription associated biomolecules to which the claims are drawn, as set forth in section 9 of the Office action mailed June 5, 2003, is withdrawn.

Information Disclosure Statement

7. The information disclosures filed August 28, 2001, January 10, 2002, and June 25, 2002 have been considered. An initialed copy of each is enclosed.

Specification

8. The disclosure is objected to for the following reason: The specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Sequences appearing in the specification and/or drawings must be identified by sequence identifier in accordance with 37 C.F.R. 1.821(d). According to 37 CFR § 1.821(a), an unbranched sequence of four or more specifically identified amino acids or an unbranched sequence of ten or more nucleotides must be identified by sequence identification numbers. See MPEP § 2422.01.

In this instance, the sequences depicted in Figure 2, namely "DPKKKRKV" and SEKDEL", are not identified by sequence identification numbers, either in the figure or in the brief description of figure at page 7. In addition, these and other sequences are disclosed elsewhere in the specification, but are not identified by a sequence identification number; see, e.g., page 24 (line 27); page 25 (lines 3 and 4); page 27 (lines 2 and 8); and page 34 (line 12). Figure 3 discloses a polynucleotide sequence that is not identified.

Applicant must provide appropriate amendments to the specification or drawings inserting the required sequence identifiers. Sequence identifiers for sequences appearing in the drawings may appear in the drawings or in the brief description of the drawings.

As noted in the attached Notice to Comply, appropriate action correcting this deficiency is required. If necessary to correct the deficiency, Applicant must submit paper and computer-readable copies of a substitute sequence listing, together with a statement that the content of both copies are the same and, where applicable, include no new matter.

9. The specification is objected to because the use of numerous improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of improperly demarcated trademarks include Geneclean™ (page 48, line 13) and Whatman™ (page 70, line 26).

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

10. The specification is objected to because the ATCC deposit accession numbers to which is referred has been omitted at page 21 (line 11), page 31 (line 4), and page 46 (lines 17 and 25).

11. The specification is objected to because "Clontech" is misspelled as "Clonetech" at page 76, line 18.

Claim Objections

12. Claims 4 and 5 are objected to because the claims recite, "selected from the group consisting **essentially** of" (emboldened for emphasis), which is improper Markush-type claim language. See MPEP § 2173.05(h).

This issue can remedied by amending claims 4 and 5 to recite, for example, "selected from the group consisting of", thus deleting "essentially".

13. Claim 20 is objected to because of the omission of "and" immediately following the semicolon in line 19 before "(d)". Appropriate correction is required.

14. Claims 21 and 22 is objected to because the claim reads, "further comprises [...]". As the claims are drawn to a kit, the claims should read, for example, "further comprising [...]", or alternatively "which further comprises [...]". Appropriate correction is required.

15. Claim 21 is objected to because the claim recites, "wherein said vector expresses said single chain antibody and is accorded as ATCC Accession No. 98483". The deposited vector is the vector designated "pVP16Zeo", which is disclosed as useful in screening a cDNA library of such polynucleotide sequences. The vector is described as containing a multiple cloning site into which a polynucleotide sequence encoding a single-chain antibody can be inserted for expression in a host cell transformed with the recombinant vector (see, e.g., Figure 5). The deposited vector is not disclosed as already comprising a polynucleotide sequence encoding a single-chain antibody; therefore, it is suggested that the claim 21 be amended to instead recite, for example, "wherein said vector is capable of expressing a single-chain antibody". Appropriate correction or rebuttal is required.

16. Claim 24 is objected to as being an improperly dependent claim. Claim 24 is drawn to a DNA construct "according to the method of claim 1", whereas claim 1 is drawn to a method for screening a DNA construct library; so claim 24 does not further

limit the subject matter of claim 1 and, moreover, claim 1 and claim 24 are not drawn to the same statutory subject matter. Furthermore, while claim 1 comprises multiple active steps that produce a DNA construct, claim 1 is not drawn to a method for producing a DNA construct; so claim 24 is not a product-by-process claim. This issue can be remedied by rewriting claim 24 in independent form and amending it recite the physical or structural properties of the DNA construct that Applicant regards as the invention.

Claim Rejections - 35 USC § 112

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 21, 22, and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 21, 22, and 54 are directed to a vector, which is accorded as ATCC Accession No. 98483.

It is unclear if a vector having the exact structural and chemical identity of the vector to which the claims refer is known and publicly available, or can be reproducibly produced or isolated without undue experimentation. Clearly, without access to the vector or a cell line comprising the vector, it would not be possible to make the claimed invention, absent a disclosure of the entire polynucleotide sequence of the vector.
The disclosure refers to a biological deposit of the vector; see, e.g., page 21 (line 11), page 31 (line 4), and page 46 (lines 17 and 25); however, these references provide insufficient assurance that all required deposits have been made and all the conditions of MPEP § 608.01 (p)(c) are met. See MPEP § 2404.03.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the original deposit was made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP § 1.804(b).

If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by Applicant or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth under 37 CFR §§ 1.801-1.809 have been met.

Furthermore, it is noted that the specification should be amended to provide specific reference to the deposited material by the name of the depository and its accession number, which further provides the depository's address and the date the deposit was made. See 37 CFR § 1.809 (d).

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims 1-7, 19, 25-29, and 50-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 and 26-29 are indefinite because claim 1 does not, nor do any of the other claims recite a positive process step and correlative that clearly relates the recited process steps and the result achieved back to the recited purpose of practicing the method. The claims are drawn to a method for screening a DNA construct library for a single chain monoclonal antibody fusion reagent capable of binding a transcription associated biomolecule within a host cell, yet no active process step refers to, or utilizes such a DNA construct library. This issue can be remedied by amending claim 1 to recite a positive process step that provides and utilizes a DNA construct library comprising DNA constructs encoding single-chain antibodies that may bind to the antigenic portion of the transcription associated biomolecule. Furthermore, although claim 1 recites, "whereby detecting said expression indicates that said fusion reagent does bind said antigenic portion within said host cell upon detection of said expression", the indication that the reagent binds the antigenic portion is not specifically correlated to the identification of a DNA construct present in the DNA construct library that encodes a single chain antibody fusion reagent capable of binding the transcription associated biomolecule. This latter issue can be remedied by amending claim 1 to recite, for example, "wherein detection of expression of said detectable gene identifies a host cell containing a DNA construct encoding a single chain monoclonal antibody fusion reagent that binds the transcription associated biomolecule within the host cell".

Claim 25 is indefinite because the claim recites, "said transcription associated biomolecule". There is no antecedent basis in the claim to support the recitation of this limitation. Because it cannot be determined to which "transcription associated biomolecule" the claim refers, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined.

Claim 25 is also indefinite because the claim recites, "said fusion reagent". There is no antecedent basis in the claim to support the recitation of this limitation. Because it cannot be determined to which "transcription associated biomolecule" the

claim refers, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined.

Claims 50, 51, and 53 are indefinite because each recites, "[t]he screening method according to claim 24"; and claim 52 is indefinite because it recites, "[t]he screening method according to claim 51". Claim 24 is drawn to a DNA construct, not a screening method. Accordingly, the nature, and the metes and bounds, of the subject matter that Applicant regards as the invention cannot be determined.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Baron et al. (*Gene*. 1992 May 15; **114** (2): 239-243), as evidenced by Apt et al. (*Mol. Gen. Genet.* 1996 Oct 16; **252** (5): 572-9).

Baron et al. teaches a shuttle vector comprising a fusion between *sh ble*, which encodes a protein that confers resistance to phleomycin and related antibiotics, and *lacZ*; see entire document (e.g., the abstract; page 241, column 2; and page 242, column 2, through page 243, column 1). Baron et al. teaches that both bacterial and fungal cells transformed with the vector can be positively selected in the presence of antibiotic; see, e.g., the abstract.

Apt et al. teaches the *sh ble* gene from *Streptoalloteichus hindustanus* encodes a protein that also confers resistance to zeocin, which is a derivative of the phleomycin; see entire document (e.g., the abstract). Therefore, as evidenced by Apt et al., the shuttle vector of Baron et al. comprises "a zeocin selective marker gene".

23. Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 5,283,173 A or Fields et al. (*Nature*. 1989 Jul 20; **340** (6230): 245-246).

Claim 24 is drawn to a DNA construct "according to the method of claim 1". As noted above, claim 1 is not drawn to a DNA construct, nor is it drawn to a method for producing a DNA construct. Nevertheless, claim 1 refers to a DNA construct, which, among others, is composed of an expression vector comprising a nucleic acid fragment encoding a DNA-binding domain peptide of a transcription activator that binds to a DNA regulatory sequence binding site. Accordingly, herein, claim 24 is drawn to such a DNA construct.

US Patent No. 5,283,173 A ('173) teaches an expression vector comprising a polynucleotide sequence encoding a DNA-binding domain peptide of a transcription activator that binds to a DNA regulatory sequence binding site; see, e.g., column 4, lines 35-44.

Fields et al. teaches a DNA construct, which is composed of an expression vector comprising a nucleic acid fragment encoding a DNA-binding domain peptide of a transcription activator that binds to a DNA regulatory sequence binding site; see entire document (e.g., page 245, column 1; and page 245, Table 1). For example, Fields et al. teaches an expression vector designated "GAL4(1-147)", which comprises the amino-terminal 147 amino acids of GAL4, which binds UAS_G (see, e.g., page 245, Table 1).

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. Claims 1, 20, 25, 27-29, and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,283,173 A in view of Hoeffler et al. (*J. Cell Biochem.* 1994; **190**: 422) (of record).

Claims 1, 25, 27-29 are drawn to a method for screening a cDNA library encoding a single-chain antibody that binds a transcription related molecule. Claims 20 and 47-49 are drawn to a kit comprising vectors and host cells for screening a cDNA library encoding a single-chain antibody that binds a transcription related molecule.

US Patent No. 5,283,173 A teaches a method for screening a cDNA library encoding a protein that binds to another protein of interest using an assay system that is now familiarly known in the art as the "yeast-two-hybrid system"; see entire document (e.g., the abstract; Figures 1 and 2; column 1, lines 15, through column 2, line 14; column 3, lines 40-43; column 5, lines 4-7; the example. '173 teaches the protein of interest is any protein, including, in particular, an antibody; see, e.g., column 1, lines 15, through column 2, line 14; and column 7, lines 42-44. '173 teaches the method comprises providing a first expression vector comprising a polynucleotide sequence encoding at least the DNA-binding domain of a DNA-binding protein fused in frame with a polynucleotide sequence encoding a protein of interest or a fragment thereof; see, e.g., column 4, lines 35-44. '173 teaches the method further comprises providing a second expression vector comprising a polynucleotide sequence encoding a protein (e.g., an antibody), which is derived from a cDNA library, fused in frame to a polynucleotide sequence encoding at least the transcription activation domain of a transcription activator; see, e.g., column 5, lines 4-27. '173 teaches both expression vectors are introduced into a host cell (e.g., a yeast cell), which comprises a detectable reporter gene that expresses a detectable protein when the detectable gene is transcriptionally activated; see, e.g., column 4, lines 21-34. '173 teaches the activation of the detectable gene occurs when the transcription activation domain of the transcription activator is brought into sufficient proximity to the DNA-binding domain of the DNA-binding protein; see, e.g., column 4, lines 30-34. '173 teaches that in the assay system, the activation of the detectable gene indicates that the second expression vector encodes a fusion protein that binds to the fusion protein encoded by the first expression vector; see, e.g., column 5, lines 9-27. Furthermore, '173 teaches a kit comprising vectors and host cells, including a first expression vector comprising a polynucleotide sequence encoding at least the DNA-binding domain of a DNA-binding

protein fused in frame with a polynucleotide sequence encoding a protein of interest or a fragment thereof, a second expression vector comprising a polynucleotide sequence encoding a protein (e.g., an antibody), which is derived from a cDNA library, fused in frame to a polynucleotide sequence encoding at least the transcription activation domain of a transcription activator, a host cell (e.g., a yeast cell), which comprises a detectable reporter gene that expresses a detectable protein when the detectable gene is transcriptionally activated once the fusion protein encoded by the first expression vector binds to the fusion protein encoded by the second expression vector, and a means for monitoring the expression of the detectable gene; see, e.g., column 5, line 28, through column 6, line 68.

'173 does not expressly teach or suggest screening a cDNA library encoding single-chain antibodies to identify a cDNA molecule encoding a single-chain antibody that binds to a protein of interest.

Hoeffler et al. teaches using the two-hybrid system in yeast, which is described by '173, to screen a cDNA library to select a clone carrying a cDNA molecule encoding a single-chain antibody that binds to a protein of interest, such as a transcription related factor.

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made to have used the method of '173 to screen a cDNA library encoding single-chain antibodies to select a clone carrying a cDNA molecule encoding an antibody that binds to a protein of interest, such as a transcription related factor, because '173 teaches the method can be used to identify a cDNA molecule encoding a protein that binds to any protein of interest, including a cDNA molecule encoding antibody, and Hoeffler et al. teaches using the methodology described by '173 to do so. One ordinarily skilled in the art at the time the invention was made would have been motivated to do so to isolate a cDNA molecule encoding encoding a single-chain antibody that binds to a protein of interest.

26. Claims 2-7, 26, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,283,173 A in view of Hoeffler et al. (*J. Cell Biochem.*

1994; **190**: 422) as applied to claims 1, 20, 25, 27-29, and 47-49 above, and further in view of Biocca et al. (*Trends Cell Biol.* 1995 June 5; **5**: 248-252).

Claims 2 and 3 are drawn to the method of claim 1 further comprising the step of fusing a polynucleotide sequence encoding an intracellular signal peptide into the coding frame of the second expression vector encoding the fusion protein comprising the antibody and activation domain and deleting the polynucleotide sequence encoding the activation domain, such that the resultant expression vector encodes a fusion protein comprising the adjoined amino acid sequences of an intracellular signal peptide and a single-chain antibody. Claims 4-7 are drawn to the methods of claim 2 or 3, wherein the transcription related molecule is selected from a group of molecules, which is recited in the claims. Claims 26 is drawn to the method of claim 1, wherein the antigenic portion of the transcription related molecule is not endogenous to the host cell. Claim 46 is drawn to the kit of claim 20, wherein the antigenic portion of the transcription related molecule is not endogenous to the host cell.

US Patent No. 5,283,173 A ('173) and Hoeffler et al. teach that which is set forth in the rejection of claims 1, 20, 25, 27-29, and 47-49 above.

Neither '173 nor Hoeffler et al. expressly teaches fusing a polynucleotide sequence encoding an intracellular signal peptide into the coding frame of the second expression vector encoding the fusion protein comprising the antibody and activation domain (claim 2) and deleting the polynucleotide sequence encoding the activation domain (claim 3), such that the resultant expression vector encodes a fusion protein comprising the adjoined amino acid sequences of an intracellular signal peptide and a single-chain antibody. Furthermore, neither reference expressly teaches selecting an antibody that binds to a transcription related molecule, such as a protein derived from an etiological agent or Ras (claims 4-7), which is not endogenous to the host cell (claims 26 and 46).

Biocca et al. review "intracellular immunization" or the intracellular expression of antibodies that bind transcription related molecules and are targeted to specific subcellular compartments; see entire document.

For example, Biocca et al. teaches fusion proteins comprising single-chain antibodies that bind human immunodeficiency virus - type 1 (HIV-1) gp120 and an intracellular signaling peptide that targets the fusion protein to the endoplasmic reticulum; see, e.g., page 249, column 1; page 250, column 1; and page 251, Tables 1 and 2. HIV-1 is an etiological agent; and gp100 is a protein derived from HIV-1 and is not endogenous to most cells, including, for example, yeast cells and mammalian cells. Biocca et al. teaches "intracellular immunization", or the intracellular expression of this fusion protein is used therapeutically since the fusion protein binds to gp100 and prevents the appearance of the viral protein on the plasma membrane to reduce the production of infectious virus (page 249, column 3, through page 250, column 1).

In addition, Biocca et al. teaches fusion proteins comprising single-chain antibodies that bind $p21^{Ras}$ (i.e., Ras) and an intracellular targeting peptide that targets the fusion protein to the cytoplasm, which when expressed intracellularly inhibits $p21^{Ras}$-dependent signal transduction and meiotic maturation; see, e.g., page 250, column 2, through column 3; and page 251, Tables 1 and 2. Human $p21^{Ras}$ is not endogenous to yeast cells, the host cells that '173 teaches are preferably used in screening the cDNA library.

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to have used the method of '173 to screen a cDNA library encoding single-chain antibodies to select a clone carrying a cDNA molecule encoding an antibody that binds to a transcription related molecule, such as HIV-1 gp100 or Ras, and then to have fused a polynucleotide sequence encoding an intracellular signal peptide that targets the endoplasmic reticulum into the coding frame of the expression vector encoding the fusion protein comprising the single-chain antibody and activation domain and deleted the polynucleotide sequence encoding the activation domain, such that the resultant expression vector encodes a fusion protein comprising the adjoined amino acid sequences of an intracellular signal peptide and a single-chain antibody, because Biocca et al. teaches or suggests that "intracellular immunization", or the intracellular expression of such a fusion protein that binds a transcription related molecule, such as gp100 or Ras, is therapeutic, since expression of the fusion protein

that binds gp100 reduces the production of infectious virus and the expression of the fusion protein that binds Ras inhibits signaling by the oncogenic protein. Accordingly, one ordinarily skilled in the art at the time of the invention would have been motivated to do so to clone fusion proteins that bind transcription related molecules, such as gp100 or Ras, because such fusion proteins interfere with the expression and activity the transcription related molecule when expressed intracellularly and targeted to appropriate subcellular compartments.

Furthermore, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to have manufactured a kit in accordance with the teachings of '173 for use in screening a cDNA library to select a cDNA clone encoding a single-chain antibody that binds transcription related molecules, such as gp100 or Ras, because Biocca et al. teaches such antibodies interfere with the expression and activity of the transcription related molecule. One ordinarily skilled in the art at the time of the invention would have been motivated to do to facilitate screening cDNA libraries to select a cDNA clone encoding a single-chain antibody that binds to a transcription related molecule, such as gp100 or Ras, since kits provide ease, convenience, and reagent uniformity.

Double Patenting

27. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

28. Claim 19 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 41-66 of copending Application No. 10/03,021. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

Claim 19 of the instant application is drawn to a shuttle vector comprising a zeocin selective marker gene.

Claims 41-66 are drawn to an expression vector or a library of expression vectors, wherein said vector or vectors comprise a marker that confers resistance to zeocin and wherein said vector or vectors are suitable for prokaryotic and eukaryotic expression; see, in particular, claims 49 and 55.

An expression vector that is suitable for expression in two different species or organisms, such as in both prokaryotic and eukaryotic organisms, is termed a "shuttle vector". Absent a showing of any difference, the shuttle vector of the instant claim and the expression vector or vectors of the copending claims are deemed the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

29. No claims are allowed.

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
October 18, 2004

Notice to Comply	Application No.	Applicant(s)	
	09/939,769	HOEFFLER ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Sequences appear in the specification that are not properly identified in accordance with 37 CFR 1.821(d); see the Office action for additional explanation. If necessary to comply, Applicants are required to submit the following:

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☐ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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